CLAIMS

We claim:

1. An isolated polynucleotide molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence having at least 80% identity to a nucleotide sequence encoding an ADAMTS-M polypeptide of SEQ ID NO: 2, or a metalloproteinase, disintegrin domain, prodomain, or thrombospondin submotif, thereof;

(b) a nucleotide sequence of at least 15 contiguous nucleotides that hybridizes under stringent conditions to the polynucleotide molecule of SEQ ID NO: 1; and

(c) the complement of the nucleotide sequence of (a) or (b).

2. An isolated polynucleotide molecule of claim 1 wherein said polynucleotide sequence comprises the ADAMTS-M polypeptide encoding sequence of SEQ ID NO: 2, or a metalloproteinase, disintegrin domain, prodomain, or thrombospondin submotif, thereof.

3. A polypeptide encoded by the isolated polynucleotide molecule of claim 1.

4. The polypeptide of claim 3 which comprises an amino acid sequence that is SEQ ID NO: 2, or a metalloproteinase, disintegrin domain, prodomain, or thrombospondin submotif, thereof.

5. An expression system comprising a DNA or RNA molecule, wherein said expression system is capable of producing an ADAMTS-M polypeptide of claim 3 when said expression system is present in a compatible host cell.

6. A host cell comprising the expression system of claim 5.

7. A process for producing an ADAMTS-M polypeptide comprising culturing a host cell of claim 6 under conditions sufficient for production of said polypeptide, and recovering the polypeptide from cell culture.

8. An agent selected from the group consisting of an antibody immunospecific for an ADAMTS-M polypeptide, an agonist for an ADAMTS-M polypeptide, an antagonist for an ADAMTS-M polypeptide, and a substrate for an ADAMTS-M polypeptide, wherein said polypeptide is the polypeptide of claim 3.

9. A method for treating a subject in need of altering activity or expression of ADAMTS-M comprising administering to said subject a therapeutically effective amount of an agent of claim 8.

10. A process for diagnosing a disease or a susceptibility to a disease in a subject related to expression or activity of ADAMTS-M in a subject comprising determining presence or absence of a mutation in a nucleotide sequence encoding a polypeptide of claim

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3 in the genome of said subject, or analyzing for presence or amount of ADAMTS-M expression in a sample derived from said subject.

11. A method for identifying compounds which antagonize, agonize, or bind to ADAMTS-M comprising:

(a) contacting a candidate compound with cells expressing an ADAMTS-M polypeptide of claim 3, or with cell membranes from cells expressing said ADAMTS-M polypeptide, or the media conditioned by cells expressing said polypeptide, or a purified composition of said polypeptide; and

(b) determining inhibition or stimulation of an ADAMTS-M activity, or binding or said candidate compound to said polypeptide.

12. A method for detecting a polynucleotide encoding ADAMTS-M in a biological sample containing nucleic acid material comprising:

(a) hybridizing an isolated polynucleotide of claim 1 that is specific to ADAMTS-M to the nucleic acid material of the biological sample, thereby forming a hybridization complex; and

(b) detecting the hybridization complex, wherein presence of the hybridization complex correlates with the presence of the polynucleotide encoding ADAMTS-M in the biological sample.

13. A method for identifying a substrate for ADAMTS-M comprising contacting a polypeptide comprising an enzymatically active polypeptide of claim 3 with a candidate substrate and determining either conversion of substrate to product or binding of the polypeptide to the substrate.

14. A method for treating arthritis (osteoarthritis and rheumatoid arthritis), inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity and rejection, cachexia, allergy, cancer (such as solid tumor cancer including colon, breast, lung, prostate, brain and hematopoietic malignancies including leukemia and lymphoma), tissue ulcerations, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joints implants, atherosclerosis (including atherosclerotic plaque rupture), aortic aneurysm (including abdominal aortic and brain aortic aneurysm), congestive heart failure, myocardial infarction, stroke, cerebral ischemia, head trauma, spinal cord injury, neurodegenerative diseases (acute and chronic), autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neuropathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, ocular angiogenesis, corneal injury, macular degeneration, abnormal wound healing, burns, infertility or diabetic shock comprising

administering a therapeutically effective amount of an agent selected from the group consisting of an agonist or antagonist of ADAMTS-M, a polypeptide of claim 3, and a polynucleotide of claim 1, in combination with a pharmaceutically acceptable carrier.

15. A pharmaceutical composition for the treatment of arthritis (osteoarthritis and rheumatoid arthritis), inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity and rejection, cachexia, allergy, cancer (such as solid tumor cancer including colon, breast, lung, prostate, brain and hematopoietic malignancies including leukemia and lymphoma), tissue ulcerations, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joints implants, atherosclerosis (including atherosclerotic plaque rupture), aortic aneurysm (including abdominal aortic and brain aortic aneurysm), congestive heart failure, myocardial infarction, stroke, cerebral ischemia, head trauma, spinal cord injury, neurodegenerative diseases (acute and chronic), autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neuropathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, ocular angiogenesis, corneal injury, macular degeneration, abnormal wound healing, burns, infertility or diabetic shock comprising a therapeutically effective amount of an agent selected from the group consisting of an agonist or antagonist of ADAMTS-M, a polypeptide of claim 3, and a polynucleotide of claim 1, in combination with a pharmaceutically acceptable carrier.